

REMARKS

Applicants respectfully requests entry of the amendments and remarks submitted herein. Claims 39 and 48 are amended, claim 51 is canceled, and claims 56-58 are added. Claims 30-50 and 52-58 are currently pending. Applicants respectfully submit that the new claims and the amendments to the claims are supported by the specification as filed and that no new matter has been added.

I. The 35 U.S.C. §112, Second Paragraph, Rejections of the Claims

The Examiner rejected claims 30-38, 45, and 48-55 under 35 U.S.C. §112, second paragraph, alleging that those claims are indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. As these rejections may be maintained with respect to the pending claims, they are respectfully traversed.

Claims 30-38

The Examiner alleges that the metes and bounds of the term "*Haemophilus influenzae*-specific lipooligosaccharide (LOS)" in claim 30 are not clear. Claim 30 recites that the DNA sequence encoding *rfe* is regulated by LsgG such that a *H. influenzae*-specific LOS is synthesized by the addition of an acceptor molecule to the terminal heptose molecule. Applicants assert that one of ordinary skill in the art would know that the *Haemophilus influenzae*-specific lipooligosaccharide (LOS) refers to the *H. influenzae*-specific LOS that is synthesized by the addition of an acceptor molecule to the terminal heptose molecule. For example, at page 4, line 23 through page 5, line 6 of the specification, Applicants teach that they have discovered that certain bacteria, such as *Escherichia coli* strain K-12, have a core liposaccharide with a terminal heptose and that bacteria containing an enzyme that catalyzes the transfer to the terminal heptose of an acceptor molecule, such as N-acetylglucosamine, can form a "scaffold" upon which glycosyltransferases add other saccharide monomers to form complex carbohydrates. Further, claim 34 recites that the acceptor molecule is N-acetylglucosamine; claim 38 recites that the bacteria further comprise a glycosyltransferase; and claim 56 recites that the glycosyltransferase is a *Haemophilus influenzae* glycosyltransferase, *i.e.*, a glycosyltransferase that can build upon the scaffold. One way to determine *Haemophilus influenzae*-specific lipooligosaccharide (LOS) is to determine whether the LOS is recognized by monoclonal antibody 6E4 (*see, e.g.*, page 10, line 23 through page 11, line 8).

Claims 48-55

The Examiner alleges that the metes and bounds of the phrase “modifying a terminal heptose of a lipopolysaccharide (LPS) or lipooligosaccharide (LOS) core structure” in claim 48 are not clear. The Examiner alleges that it is not clear whether adding an N-acetyl glucosamine to the terminal heptose is "modifying" the heptose or if other "modifications" are encompassed by the phrase. Claim 48 is amended to more specifically recite that that an N-acetyl glucosamine is added onto the terminal heptose so as to modify the terminal heptose. Claim 51 is canceled.

Claims 36, 45 and 53

The Examiner alleges that the metes and bounds of the phrase “*rfe* is part of the gram-negative bacterial genome” are not clear. The Examiner indicates that it is not clear what is meant by the term "part". Applicants respectfully submit that the phrase “*rfe* is part of the gram-negative bacterial genome” indicates to the art worker that the *rfe* is endogenous to the genome of the gram-negative bacteria.

Thus, Applicants respectfully request that the rejections under 35 U.S.C. §112, second paragraph, be withdrawn.

II. The 35 U.S.C. §112, First Paragraph (Written Description) Rejection of the Claims

The Examiner rejected claims 30-55 under 35 U.S.C. §112, first paragraph, alleging that those claims fail to comply with the written description requirement. As this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

Independent claim 30 recites a process for the production of a *Haemophilus influenzae*-specific lipooligosaccharide (LOS) which comprises the steps of: (a) growing in a culture medium gram-negative bacteria comprising (i) a core lipid structure containing a terminal heptose and (ii) a DNA sequence encoding an Undecaprenyl-phosphate N-acetyl glucosaminyl phosphate transferase (*rfe*), and (iii) an isolated DNA sequence encoding a lipooligosaccharide-synthesis gene G polypeptide (LsgG) from *Haemophilus influenzae*, wherein the DNA sequence encoding *rfe* is regulated by LsgG such that a *H. influenzae*-specific LOS is synthesized by the addition of an acceptor molecule to the terminal heptose molecule; and (b) recovering the *H. influenzae*-specific LOS from the culture medium. Claims 31-38 and 56 ultimately depend from claim 30.

Independent claim 39 recites a process for the production of a complex carbohydrate comprising the steps of: (a) growing in a culture medium gram-negative bacteria comprising (i) a core lipid structure containing a terminal heptose and (ii) a DNA sequence encoding an Undecaprenyl-phosphate N-acetyl glucosaminyl phosphate transferase (*rfe*), and (iii) an isolated DNA sequence encoding a lipooligosaccharide-synthesis gene G polypeptide (LsgG) from *Haemophilus influenzae*, wherein the DNA sequence encoding *rfe* is regulated by LsgG such that a complex carbohydrate is synthesized by the addition of an acceptor molecule to the heptose molecule; and (b) recovering the complex carbohydrate from the culture medium. Claims 40-47 and 57 ultimately depend from claim 39.

Independent claim 48 recites a method comprising modifying a terminal heptose of a lipopolysaccharide (LPS) or lipooligosaccharide (LOS) core structure of a gram-negative bacterial species, wherein the gram-negative bacterial species comprises a polynucleotide encoding an Undecaprenyl-phosphate N-acetyl glucosaminyl phosphate transferase (*rfe*) and an isolated DNA sequence encoding a lipooligosaccharide-synthesis gene G polypeptide (LsgG) from *Haemophilus influenzae*, wherein the polynucleotide encoding *rfe* is regulated by lipooligosaccharide-synthesis gene G polypeptide (LsgG) from *Haemophilus influenzae* such that an N-acetyl glucosamine is added onto the terminal heptose so as to modify the terminal heptose, wherein the gram-negative bacterial species is *Salmonella minnesota*. Claims 49, 50, 52-55 and 58 ultimately depend from claim 49. Claim 51 is canceled.

Applicants assert that the specification as originally filed provides an adequate written description of the claimed invention. Applicants may show adequate written description by demonstrating that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics that provide evidence that Applicant was in possession of the claimed invention, *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. *Enzo Biochem. v. Gen-Probe Inc.*, 323 F.3d 956, 963, 63 U.S.P.Q.2d 1609, 1613 (Fed. Cir. 2002). What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.3d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986). Furthermore, the written description requirement states that the Applicants must describe the invention; it does not state that every

invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution. *Capon v. Eshhar v. Dudas*, 2005 U.S. App. LEXIS 16865 (Fed. Cir. 2005). Moreover, it is not necessary that every permutation within a generally operable invention be effective in order to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention. *Capon v. Eshhar v. Dudas*, 2005 U.S. App. LEXIS 16865 (Fed. Cir. 2005).

The Examiner alleges that the specification fails to describe a representative species of the genus comprising any or all polynucleotides encoding *rfe* and the genus comprising any or all polynucleotides encoding *lsgG* used to transform a genus comprising any or all gram-negative bacteria.

Applicants have discovered that gram-negative bacteria, such as *Escherichia coli*, have a core lipid structure with a terminal heptose and that such bacteria, when they contain an enzyme which catalyzes a transfer to the terminal heptose of an acceptor molecule (*i.e.*, the protein encoded by *rfe*), can form a "scaffold" upon which glycosyltransferases can add other saccharide monomers. Applicants have also discovered that LsgG increases the expression from *rfe*, thereby allowing for the regulation of *rfe* with LsgG. Accordingly, Applicants have claimed methods that include the use of gram-negative bacteria that contain: (1) a core lipid structure containing a terminal heptose; (2) a sequence encoding an Undecaprenyl-phosphate N-acetyl glucosaminyl phosphate transferase (*rfe*); and (3) an isolated sequence encoding a lipooligosaccharide-synthesis gene G polypeptide (LsgG) from *Haemophilus influenzae*. The claims further recite that the DNA sequence encoding *rfe* is regulated by LsgG such that an acceptor molecule (*e.g.*, N-acetylglucosamine) is added to the terminal heptose molecule.

Applicants provide structural characteristics of the bacteria and DNA sequences recited in the claims. For example, the claims recite that the gram-negative bacteria used in the methods comprise a DNA sequence encoding an Undecaprenyl-phosphate N-acetyl glucosaminyl phosphate transferase (*rfe*). The *rfe* may be, *e.g.*, a part of the gram-negative bacterial genome or may be from a different source, such as from *Haemophilus influenzae*. The Examiner is requested to note that gram-negative bacterial species that contain an *rfe* gene can be employed in the methods of the invention. For example, *rfe* is present in various *E. coli* strains (*e.g.*, K-12, O18, O75 and O111), in *Klebsiella pneumoniae* and *Salmonella minnesota*. For example, Dr. Apicella's Declaration, submitted on

November 06, 2001, demonstrates the feasibility of using *Salmonella minnesota* to make complex carbohydrates with the *lsg* locus. Additionally, the specification discloses at page 4, line 29 through page 5, line 1 that *rfe* from *Haemophilus influenzae* may be used. At page 6, lines 6-8, the specification discloses that the *rfe* sequence from *Haemophilus influenzae* is available in the TIGR database. Further searching of the TIGR database for *rfe* genes revealed that an *rfe* gene, at the time the application was filed, was known to the art worker in *Aquifex aeolicus*. Moreover, Cole et al. had previously disclosed the sequence of the *rfe* protein from *Mycobacterium tuberculosis* (Cole et al., *Nature*, 393, 537-544 (1998)). Thus, Applicants disclosures in the specification as filed with respect to the *rfe* sequence, when read in the context of what was known to the art worker, satisfies the written description requirement of 35 U.S.C. §112, first paragraph.

The claims also recite that the gram-negative bacteria used in the methods comprise an isolated DNA sequence encoding a lipooligosaccharide-synthesis gene G polypeptide (LsgG) from *Haemophilus influenzae* (emphasis added). At page 6, lines 6-8, the specification discloses that a *lsgG* sequence from *Haemophilus influenzae* is available in the TIGR database. Thus, Applicants disclosures in the specification as filed with respect to the *lsgG* sequence, when read in the context of what was known to the art worker, satisfies the written description requirement of 35 U.S.C. §112, first paragraph.

Furthermore, in addition to the experiments using *E. coli* described in the specification, Dr. Apicella's Declaration, submitted on November 06, 2001, demonstrates the feasibility of using *Salmonella minnesota* to make complex carbohydrates with the *lsg* locus. Claim 48 has been amended to recite that the gram-negative bacterial species is *Salmonella minnesota*. Applicants respectfully submit that the art worker, at the time the application was filed, was well apprised of gram-negative bacteria other than *E. coli* and *Salmonella minnesota* that could be used in the methods recited in claims 30 and 39.

Applicant also provides functional characteristics of the bacteria and DNA sequences recited in the claims, namely, that the DNA sequence encoding *rfe* is regulated by LsgG such that a *H. influenzae*-specific LOS is synthesized by the addition of an acceptor molecule to the terminal heptose molecule (claim 30); the DNA sequence encoding *rfe* is regulated by LsgG such that a complex carbohydrate is synthesized by the addition of an acceptor molecule to the heptose molecule (claim 38); and the polynucleotide encoding *rfe* is regulated by lipooligosaccharide-

synthesis gene G polypeptide (LsgG) from *Haemophilus influenzae* such that an N-acetyl glucosamine is added onto the terminal heptose so as to modify the terminal heptose. Thus, Applicant provides the art worker with functional characteristics of the bacteria and DNA sequences recited in the claims.

To the extent that the Examiner's rejection may be made based on the allegation that the claims encompass inoperative embodiments, the Examiner is requested to note that claims are in accord with the requirements of 35 U.S.C. § 112 if one of skill in the art, guided by the specification, could avoid inoperable combinations and practice the invention without undue experimentation. The mere possibility that a claim embraces inoperable embodiments does not render it unduly broad. In addition, it is not a function of the claims to specifically exclude all possible inoperative substances. Applicants respectfully submit that one of skill in the art, guided by the specification, could avoid inoperable combinations and practice the invention without undue experimentation.

Applicants thus respectfully assert that sufficient details of the identifying structural and functional characteristics of the methods have been provided or were available to one of ordinary skill in the art at the time the application was filed, and as such, Applicants were in possession of the full scope of the claimed invention at the time the application was filed.

III. The 35 U.S.C. §112, First Paragraph (Enablement) Rejection of the Claims

The Examiner rejected claims 30-55 under 35 U.S.C. §112, first paragraph, alleging that those claims fail to comply with the enablement requirement. As this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

The Examiner alleges at page 10 of the Office Action that the specification does not enable the present scope of the claims because the specification does not establish (A) regions of the encoded protein whose structure which may be modified without affecting its activity of synthesizing *Haemophilus influenzae* specific LOS in gram-negative bacteria normally producing only LPS; (B) the general tolerance of said proteins to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue on these proteins with an expectation of obtaining the desired biological function; (D) a universal method of producing *Haemophilus influenzae* specific LOS in gram-negative bacteria normally producing only LPS; and

(E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

When rejecting a claim under the enablement requirement of 35 U.S.C. §112, the Examiner bears the initial burden of setting forth a reasonable explanation as to why he or she believes that the scope of protection provided by the claims is not adequately enabled by the description of the invention provided in the specification.” *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The Examiner bears the burden of providing evidence or technical reasoning to substantiate doubts that the specification is not enabling with respect to the scope of a claim sought to be patented. *Ibid.* See also MPEP § 2164.04. Without evidence or technical reasoning to doubt the truth of the statements made in the application, the application must be considered enabling. *Ibid.*

Applicants have discovered that gram-negative bacteria, such as *Escherichia coli*, have a core lipid structure with a terminal heptose and that such bacteria, when they contain an enzyme which catalyzes a transfer to the terminal heptose of an acceptor molecule (*i.e.*, the protein encoded by *rfe*), can form a "scaffold" upon which glycosyltransferases can add other saccharide monomers. Applicants have also discovered that LsgG increases the expression from *rfe*, thereby allowing for the regulation of *rfe* with LsgG. Accordingly, Applicants have claimed methods that include the use of gram-negative bacteria that contain: (1) a core lipid structure containing a terminal heptose; (2) a sequence encoding an Undecaprenyl-phosphate N-acetyl glucosaminyl phosphate transferase (*rfe*); and (3) an isolated sequence encoding a lipooligosaccharide-synthesis gene G polypeptide (LsgG) from *Haemophilus influenzae*. The claims further recite that the DNA sequence encoding *rfe* is regulated by LsgG such that an acceptor molecule (*e.g.*, N-acetylglucosamine) is added to the terminal heptose molecule. Applicants have also demonstrated such methods in *Escherichia coli* (see the specification) and in *Salmonella minnesota* (see the Declaration submitted November 06, 2001). As detailed hereinabove in the remarks to the written description rejection, Applicants have provided both structural features of the *rfe* and *lsgG* sequences used in the method claims and have also recited a functional relationship between those sequences, namely that the *rfe* is regulated by LsgG.

When analyzing whether “undue experimentation” is required to practice claimed methods, the key word is “undue” not “experimentation.” *In re Angstadt*, 190 U.S.P.Q. 214, 219 (C.C.P.A.

1976). Enablement is not precluded by the necessity for some experimentation, such as performing routine assays. In fact, a considerable amount of experimentation is permissible if the experimentation is merely routine, or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should take. *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (Bd. App. 1982).

Applicants disclosures in the specification and in the Declaration, when read in the context of what was known to the art worker, satisfies the enablement requirement of 35 U.S.C. §112, first paragraph, because any experimentation needed would not be undue.

Further, the presence of potentially inoperative embodiments within the scope of a claim does not necessarily render a claim non-enabled. The proper standard is whether a skilled person could determine which embodiments would be operative or inoperative with expenditure of no more effort than is normally required in the art. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984). A considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.” *In re Wands*, 858 F.2d 731, 737, 8 USPQ 2d 1400, 1404 (Fed. Cir. 1988). Time and expense are merely factors in this consideration and are not controlling factors. *United States v. Telectronics, Inc.* 857 F.2d 778, 785 (Fed. Cir. 1988).

Thus, Applicants respectfully submit that the claims satisfy the enablement requirement of 35 U.S.C. §112, first paragraph.

IV. The 35 U.S.C. §102(b) Rejection of the Claims

The Examiner rejected claims 30-34, 36-41, 43, 45-50, and 53-55 under 35 U.S.C. §102(b), alleging that those claims are anticipated by McLaughlin et al. (*Journal of Endotoxin Research*, 1, 165-174 (1994); hereinafter McLaughlin). As this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

A rejection of anticipation under 35 U.S.C. § 102 requires the disclosure in a single prior art reference of each element of the claim under consideration. *In re Dillon*, 919 F.2d 688, 16 U.S.P.Q.2d 1897, 1908 (Fed. Cir. 1990) (en banc), cert. denied, 500 U.S. 904 (1991). For anticipation, there must be no difference between the claimed invention and the reference disclosure,

as viewed by a person of ordinary skill in the art. *Scripps Clinic & Res. Found. v. Genentech, Inc.*, 927 F.2d 1565, 18 USPQ2d 101 (Fed. Cir. 1991). To overcome the defense of anticipation, "it is only necessary for the patentee to show some tangible difference between the invention and the prior art." *Del Mar Engineering Lab v. Physio-Tronics, Inc.*, 642 F.2d 1167, 1172, (9th Cir. 1981). Applicants respectfully submit that the claims are not anticipated by the cited document.

Independent claims 30, 39 and 48 are described hereinabove. Claims 31-34, 36-38 and 56 ultimately depend from claim 30. Claims 40-41, 43, 45-46 and 57 ultimately depend from claim 39. Claims 49-50, 53-55 and 58 ultimately depend from claim 48.

The Examiner is respectfully requested to note that claims 30 and 39 recite the step of recovering *H. influenzae*-specific LOS from the culture medium (claim 30) or recovering complex carbohydrate from the culture medium (claim 39). McLaughlin relates to the DNA sequence analysis of the *lsg* cluster and to the analysis of proteins encoded by the *lsg* cluster (*see, e.g.*, the Summary). Applicants respectfully submit that McLaughlin does not teach recovering *H. influenzae*-specific LOS or complex carbohydrate from culture medium as recited in the present claims.

Further, claim 48 recites the use of *Salmonella minnesota*, which was previously recited in claim 51. The Examiner did not reject claim 51 under 35 U.S.C. §102(b). McLaughlin does not teach the use of *Salmonella minnesota*.

Accordingly, because McLaughlin lacks the disclosure of each element of the claims under consideration, withdraw of the rejection of the claims under 35 U.S.C. § 102 is appropriate and is respectfully requested.

V. Claims Rejections under 35 U.S.C. §103(a)

Claims 33, 35, 42, 44, and 51-52 are rejected under 35 U.S.C. §102(b) as being unpatentable over McLaughlin in view of Preston et al. (*Critical Reviews in Microbiology*, 22, 139-180 (1996); hereinafter Preston) and Swierzko et al. (*Infection and Immunity*, 61, 3216-3221 (1993); hereinafter Swierzko). As this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

A rejection of obviousness under 35 U.S.C. § 103 requires that the Examiner establish a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, the Examiner has

the burden to establish three basic elements. First, the Examiner must establish that there is some suggestion or motivation, either in the cited documents themselves or in the knowledge generally available to an art worker, to modify the documents or to combine document teachings so as to arrive at the claimed invention. Second, the Examiner must establish that there is a reasonable expectation of success. Finally, the Examiner must establish that the prior art documents teach or suggests all the claim limitations. M.P.E.P. 2143.

Applicants respectfully submit that the Examiner has not demonstrated that the claims are *prima facie* obvious in view of the cited documents, for example, because the Examiner has not established the suggestion or motivation, either in the cited documents themselves or in the knowledge generally available to an art worker, to modify the documents or to combine document teachings so as to arrive at the claimed invention.

The Examiner states at page 14 of the Office Action that McLaughlin does not teach a method of transforming *Salmonella minnesota* with a polynucleotide encoding a *rfe* from *H. influenzae*. McLaughlin specifically relates to the DNA sequence analysis of the *lsg* cluster and to the analysis of proteins encoded by the *lsg* cluster (*see, e.g.*, the Summary). Applicants respectfully submit that McLaughlin does not teach recovering *H. influenzae*-specific LOS or complex carbohydrate from culture medium as recited in the present claims. Further, there is nothing in McLaughlin that discloses *rfe*, let alone the recited interaction between *rfe* and LsgG. Rather, Applicants respectfully submit that McLaughlin was not at all sure of what the ORFs in the *lsg* cluster encoded, which is evident when McLaughlin concludes at page 174 that "future studies will be directed at defining the functions of the proteins expressed by the ORFs within this locus".

The Examiner refers to Table 4 on page 154 of Preston. However, Table 4 simply lists the *lsg* locus of *H. influenzae* and lists the function/comment with the *lsg* locus of expression of 6E4 epitope and lists *H. influenzae rfe* as being a homolog of LOS/LPS biosynthetic genes of other organisms. Alexander et al. (*Journal of Bacteriology*, 176, 7079-7084 (1994) discloses that *rfe* is involved in the biosynthesis of enterobacterial common antigen (ECA), the biosynthesis of the O7 repeat of *E. coli* as well as other O-specific polysaccharides (page 7079, right hand column). As Preston teaches, LOS molecules are not the same as ECA O7 repeats or other O-specific polysaccharides (*see* Preston at pages 139-141 and 145).

Swierzko discloses the serological characterization of antisera collected from rabbits immunized with heat-killed *Salmonella minnesota* R4 chemotype Rd₂P⁻ (see Abstract and page 3218).

Applicants respectfully submit that the Examiner has not established a motivation, nor the expectation of success, for using gram-negative bacteria that contain: (1) a core lipid structure containing a terminal heptose; (2) a sequence encoding an Undecaprenyl-phosphate N-acetyl glucosaminyl phosphate transferase (*rfe*); and (3) an isolated sequence encoding a lipooligosaccharide-synthesis gene G polypeptide (LsgG) from *Haemophilus influenzae* for producing and recovering *H. influenzae*-specific LOS (claim 30) or complex carbohydrate (claim 39) or a method comprising modifying a terminal heptose of a LPS or LOS core structure of a gram-negative bacterial species, wherein the gram-negative bacterial species comprises a polynucleotide encoding *rfe* and an isolated DNA sequence encoding a LsgG from *Haemophilus influenzae*, wherein the polynucleotide encoding *rfe* is regulated by LsgG such that an N-acetyl glucosamine is added onto the terminal heptose so as to modify the terminal heptose, wherein the gram-negative bacterial species is *Salmonella minnesota* (claim 48). In particular, the Examiner has not provided the motivation to specifically combine *rfe* and *Haemophilus influenzae* LsgG in the gram-negative bacteria so as to perform the recited methods, as Applicants discovered that *rfe* is regulated by LsgG.

Thus, Applicant respectfully submits that the cited documents, neither alone nor in combination, teach the claimed invention.

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CONCLUSION

Applicants respectfully submit that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicants' attorney at (952) 876-4094 to facilitate prosecution of this application.

If necessary, please apply any charges or credits to Deposit Account No. 50-3503.

Respectfully submitted,

Michael A. Apicella et al.

By their Representatives,

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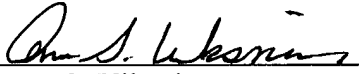
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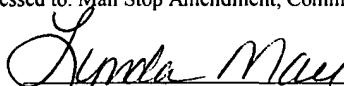
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